REMARKS

Summary of Invention

The invention features *lin-37* nucleic acids encoding polypeptides capable of altering cellular proliferation and vectors and host cells containing these nucleic acids.

Summary of Office Action

Examination of claims 1, 4-7, 10-18, 25, and 34-64 is reported in the present Office Action. Claims 1, 4-7, 10-18, 25, and 34-64 are rejected under 35 U.S.C. § 101. Claims 1, 4-7, 10-18, 25, and 34-64 are further rejected under 35 U.S.C. § 112, first paragraph. Each of the rejections is addressed below.

Information Disclosure Statement

Applicants note that the Form PTO-1449, submitted on April 13, 2000, has not been initialed, and request that the initialed Form PTO-1449 be returned with the next Office Action.

Support for the Amendment

Support for the amendment of claims 1, 7, 10, 16, 18, 25, 34, 40, 46, and 52, which now recite "hydrophilic, acts non-cell autonomously, and inhibits cell proliferation" is provided at Figures 21 and 22, which show that LIN-37 is hydrophilic and acts non-cell autonomously, respectively; and at page 9, lines 16-21, where applicants disclose that SynMuv genes are "characterized by their ability to modulate cell proliferation," and at page 10, lines 8-10, where applicants disclose that modulating cell proliferation means "increasing or decreasing the number of cells which undergo cell division in a given cell population or altering the fate of a given cell."

Support for the amendment of claims 1, 10, 16, 18, 25, 34, 46, 52, 58, and 61, which now recite "at least 85% amino acid sequence identity to SEQ ID NO:1," is found at page 10, line 22.

Support for the amendment of claims 58 and 61, which now recite "a decreased level of cell proliferation," is found at page 10, lines 15-16, where applicants state, "By 'inhibiting cell proliferation' is meant any decrease in the number of cells which undergo division relative to an untreated control."

Rejections under 35 U.S.C. § 101

The Examiner rejects claims 1, 4-7, 10-18, 25, and 34-64 as lacking utility. The rejected claims feature *lin-37* nucleic acids and vectors and host cells comprising these nucleic acids. The Office asserts:

> There is no *evidence of record* that there is any demonstrated real world use for the *lin-37* protein obtained from *C. elegans*. (Office Action mailed October 22, 2002, p. 3., first paragraph, emphasis added.)

The requirement that applicants provide evidence with respect to an asserted utility, has no basis in case law. An applicant is not required to provide evidence of utility; an applicant's assertion of utility creates a presumption of utility that satisfies the utility requirement of 35 U.S.C. § 101. *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). On this point, Applicants disclose that SynMuv nucleic acids, such as *lin-37*, are useful for identifying homologs in other species (page 16, line 22, to page 17, line 3); for identifying candidate compounds that modulate SynMuv expression (page 28, lines 11, to page 29, line 10); and for identifying candidate compounds that modulate cell death activity (page 29, lines 11-17). Molecules discovered to be effective modulators of Synmuv expression or activity can then be tested in animal models (page 29, lines 22-23). In addition, SynMuv nucleic acids are useful in modulating cell proliferation (pages 30-31) and as diagnostics for detecting aberrant levels of cell proliferation (pages 33-36).

It is the Examiner who bears the burden of providing countervailing evidence showing that the skilled artisan would doubt the veracity of applicants' assertion of utility.

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless *countervailing evidence*

> can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. (M.P.E.P. 2107 II D) (Emphasis added.)

The Examiner has failed to provide such evidence.

Applicants direct the Office's attention to *In re Langer*, 503 F.2d at 1391, 183 USPQ at 297:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope. (Emphasis in original.)

Applicants have clearly disclosed a specific utility for their claimed invention. *lin-37* functions in the *C. elegans* synMuv pathway, which is an evolutionarily conserved tumor suppressor pathway. In *C. elegans, lin-37* regulates the highly conserved Ras signal transduction pathway, and thus modulates vulval cell proliferation; mammalian homologs of *lin-37* will undoubtedly fulfill a similar regulatory function in mammalian cell proliferation. Given this function, applicants disclose, as detailed above, that *lin-37* nucleic acid molecules are useful for identifying homologs in other species (page 16, line 22, to page 17, line 3), for drug screening (pages 28-29), for gene therapy (pages 30-31), and as diagnostics (pages 33-36).

The Examiner implies that applicants' claimed invention lacks utility because the discovery was made in a model organism, and that, in the absence of evidence to the contrary, such discoveries are inherently lacking in utility. Applicants have shown that the skilled artisan accepts that SynMuv nucleic acids have utility as evidenced in Exhibits A-C, provided in the Supplemental Reply mailed on July 8, 2002. Moreover, discoveries made in *C. elegans* are generally accepted as having a real world utility as evidenced by Dr. Horvitz's recent acceptance of the 2002 Nobel Prize in Physiology or Medicine, which is awarded only to those who "shall have conferred the greatest benefit on mankind (Alfred Nobel)." In part, this award was conferred upon Dr. Horvitz for the

relevance of his discovery of *C. elegans* genes. Applicants have provided ample evidence supporting the fact that the skilled artisan accepts the utility of *C. elegans* SynMuv nucleic acids. Nothing more is required to meet the 35 U.S.C. § 101 utility requirement.

The Office states: "the asserted utilities are speculative, inviting the artisan to elaborate a functional use for the disclosed nucleic acids...(Office Action mailed October 22, 2002, page 3, lines 6-7)." With respect to such statements the Office's guidelines are unambiguous. "Office personnel should be careful, however, not to label certain types of inventions as "incredible" or "speculative" as such labels do *not* provide the correct focus for the evaluation of an assertion of utility (M.P.E.P. 2107.02 III B)." Rather the M.P.E.P. cautions, "Rejections under 35 U.S.C. § 101 have been rarely sustained by federal courts."

Again, the Examiner is reminded that the burden of proof in supporting a lack of utility rejection is on the Examiner.

> [T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability...If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the *applicant is entitled to grant of the patent* (emphasis added). *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992)

No evidence has been made of record in this case that would cause one to doubt applicants' assertion that *lin-37* nucleic acids and polypeptides are useful for the modulation of cell proliferation. In contrast, applicants have provided compelling evidence supporting the utility of the claimed invention. Thus, the utility rejection should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Applicants note that the Examiner identified the rejected claims as 1, 4-7, 10-18, 25, and 36-64. This appears to reflect a typographical error. Applicants' reply addresses

the rejection of claims 1, 4-7, 10-18, 25, and 34-64 under 35 U.S.C. § 112, first paragraph, as lacking utility, and for failing to provide an adequate written description.

Claims 1, 3-7, 10-18, 25, and 34-64 stand further rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time of filing. The claims relate to *lin-37* nucleic acids and vectors and host cells containing these nucleic acids. This rejection may be withdrawn in view of the present amendments and comments below.

To provide an adequate "written description," applicants need only communicate to those skilled in the art that the claimed subject matter is intended to be part of their invention. As stated by the Federal Circuit in *Martin v. Mayer*, 823 F.2d 500, 3 U.S.P.Q.2d 1333 (Fed. Cir. 1987):

> [T]he specification must 'convey clearly to those skilled in the art to whom it is addressed...the information that [the inventor] has invented the specific subject matter later claimed

Applicants submit that they have clearly satisfied this standard. The invention features nucleic acids comprising a *lin-37* gene family that is identified by specific structural and functional characteristics, as well as vectors and host cells comprising these nucleic acids. Claims 1, 7, 34, and their dependent claims, feature nucleic acids encoding an amino acid sequence having at least 85% or greater nucleic acid sequence identity to SEQ ID NO:2, where the polypeptide is hydrophilic, acts non-cell autonomously, and inhibits cell proliferation. Claims 10, 25, 34, 40, 58, 61, and their dependent claims, feature nucleic acids having at least 85% nucleotide sequence identity to SEQ ID NO:2, where the nucleic acid encodes a polypeptide that is hydrophilic, acts non-cell autonomously, and inhibits cell proliferation. Claims 15, 16, 18, 46, and 52 provide vectors and host cells comprising these nucleic acids.

The Examiner's attention is directed to applicants' specification, where applicants disclose the structural and functional characteristics of *lin-37* nucleic acids and polypeptides. For example, at Figure 3 applicants disclose an exemplary *lin-37* nucleic

acid molecule (SEQ ID NO:2). Applicants disclose characteristic features of LIN-37 polypeptides at Figure 21, which shows that LIN-37 polypeptides are hydrophilic, and at Figure 22, where applicants teach that LIN-37 polypeptides act non-cell autonomously. In addition, applicants disclose that LIN-37 polypeptides function in cell proliferation (page 9, lines 16-21).

In sum, applicants disclose an exemplary *lin-37* nucleic acid molecule, SEQ ID NO:2; describe characteristic features common to all *lin-37* polypeptides (e.g., hydrophilicity and a non-cell autonomous mode of action); and disclose that LIN-37 polypeptides function in cellular proliferation. Provided with applicants' disclosure, one skilled in the art would certainly recognize and appreciate that applicants' invention encompasses a *lin-37* gene family, and it is this description that also allows the skilled artisan to identify and recognize other species falling within the present claims. Applicants' specification therefore provides a description of the class of DNA molecules encompassed by the present claims. Thus, the § 112 rejection should be withdrawn.

Information Disclosure Statement

Applicants also draw the Examiner's attention to the Information Disclosure Statement mailed on April 13, 2000, and request that the Form PTO-1449 submitted with that statement be initialed and returned with the next Action.

CONCLUSION

Applicants submit that this case is in condition for allowance, and such action is respectfully requested. If the Office does not concur, a telephonic interview with the undersigned is hereby requested.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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